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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,826	09/07/2000	Axel Ullrich	205884	1983

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EXAMINER
MURPHY, JOSEPH F

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/600,826	Applicant(s) ULLRICH ET AL.	
	Examiner Joseph F Murphy	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-65* is/are pending in the application.

4a) Of the above claim(s) *35-46 and 55-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,7,8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claims 47-54 in Paper No. 12/9/2002 is acknowledged. The traversal is on the ground(s) that there is a corresponding special technical feature which defines a contribution over the prior art. This is not found persuasive because Applicant's submission of the instant application as a 371 is acknowledged, however the first claim 47 does not provide a technical feature that is distinguished over the prior art, as evidenced by Neilson et al. (1996), which discloses mutant FGF receptors. Therefore, the instant invention lacks Unity of Invention and restriction is set forth as it applies to U.S. practice.

The requirement is still deemed proper and is therefore made FINAL.

Sequence Rules

According to 37 CFR 1.821(d) (MPEP § 2422), where the description or claims of a patent application discuss a sequence listing that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the assigned identifier, in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application. Sequences appear on page 9, first paragraph of the specification but are not identified by SEQ ID NO as required.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 47-54 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are directed to mutated FGFR-4 and DNA encoding such a receptor. However, none of the claims are drawn to isolated protein or DNA, and thus read on a product of nature.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid which has been deposited as Gene Bank Accession X57205 (Specification at 9), and the polypeptide which is encoded by the deposited nucleic acid, does not reasonably provide enablement for a nucleic acid encoding an FGFR-4 polypeptide or a mutant FGFR-4 polypeptide, an FGFR-4 polypeptide, or a mutated FGFR-4 polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 47-54 are overly broad since insufficient guidance is provided as to which of the myriad of variant polypeptides that will retain the characteristics of FGFR-4 activity. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors considered to be relevant in the instant case are set forth below:

(1) the breadth of the claims - The claims are drawn to a nucleic acid encoding any mutated FGFR-4 polypeptide mutated in any way, and the mutated polypeptide wherein the mutated protein has an altered activity. There is no definition set forth for what the altered activity must be.

(2) the nature of the invention – The invention is a nucleic acid and the encoded protein.

(3) the state of the prior art – Neilson et al. (1996) teaches that mutations of FGFR-1, 2 and 3 which are expected to produce constitutive activation have that effect (Neilson at 25055, first column first paragraph). However, there are subtle functional differences for these mutations (page 25057, column 1, first paragraph).

(5) the level of predictability in the art – The specification on page 3, third paragraph discloses that there is only one known protein product for FGFR-4, and that because of the lack in many protein products of the specificity for defined FGF's, it is difficult to determine the action of a specific ligand on a specific receptor, thus there is no correlation between FGFR-4 structure and any altered activity.

(6) the amount of direction provided by the inventor - Applicant has only taught the deposited nucleic acid of X57205, and the protein encoded thereby. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of FGFR-4. As set forth in the specification, there is a lack in many protein products for a specificity for defined FGF's, thus there is no correlation between FGFR-4 structure and any altered activity.

(7) the existence of working examples - Working examples are provided for the polypeptide encoded by the deposited nucleic acid of X57205, and the protein encoded thereby.

(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. As demonstrated by the specification, there is a lack in many protein products for a specificity for defined FGF's, thus there is no correlation between FGFR-4 structure and any altered activity. The amino acid sequence of a polypeptide determines its structural and functional properties, and predictability of which amino acids can be substituted is extremely complex and well outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since the claims encompass variant polypeptides, and the nucleic acids encoding the mutated polypeptides, and given the art recognized unpredictability of the effect of mutations on protein function, and the indefinite nature of the activity which is to be altered, it would require undue experimentation to make and use the claimed invention.

Given the breadth of claims 47-54 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claims 47-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The claims are drawn to a nucleic acid encoding an FGFR-4 polypeptide or a mutant FGFR-4 polypeptide, an FGFR-4 polypeptide, or a mutated FGFR-4 polypeptide. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the polypeptide encoded by the deposited nucleic acid of X57205. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the polypeptide encoded by the deposited nucleic acid of X57205 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 47-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 49 recites the limitation "the transmembrane domain". There is insufficient antecedent basis for this limitation in the claim.

The term "altered" in claim 47 is a relative term which renders the claim indefinite. The term "altered" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. Claims 48-54 are rejected insofar as they depend on the recitation of the term "altered" in claim 47.

Claims 47-54 are vague and indefinite in the recitation of the terms "FGFR-4". There is no definition within the claim to define the protein to which these acronyms refer. Thus, the metes and bounds of this claim cannot be determined.

Claim 50 is vague and indefinite in the recitation of "amino acid 388" because no direction is provided as to the sequence of which amino acid 388 is mutated.

Claim 50 is vague and indefinite in the recitation of the term "optionally". Either the substitution is present, or it is not. It is not clear under what conditions and circumstances it would be present and not present with regard to the term "optionally".

Claim 48 is vague and indefinite in the recitation of the term "wild-type receptor" because no definition is provided to define the sequence of the receptor which is to be considered "wild-type".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 47-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Neilson et al. (1996).

Neilson et al. teaches mutated Xenopus FGF receptors (page 25050, column 1, second paragraph and page 25051, Figure 1). Given the indefinite nature of the term FGFR-4 (see the rejection under 35 USC § 112 second paragraph, *supra*), the mutant FGF receptor proteins taught in Neilson (page 25052, Figure 2) anticipate claims 47-50. The nucleic acids encoding the mutant FGF receptors (page 25050, column 1, fourth paragraph) anticipate claims 51-54.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
March 3, 2003

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